

02 sub B2
9(amended). A composition for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition [comprising] consisting essentially 30 to 60 percent alpha acids and 15 to 45 percent beta acids.

Please cancel claims 5, 11, 14, and 18-42.

REMARKS

All amendments are made to particularly specify the present invention and support can be found throughout the specification. No new matter is added in the amendment.

ELECTION OF RESTRICTION REQUIREMENT

The Examiner has required that the claimed invention be restricted under 35 U.S.C. § 121, to:

- I Claims 1-42, drawn to a composition, classified in class 424, subclass 750.
- II Claims 43-47, drawn to a first method of using the composition, classified in class 514, subclass 783.
- III. Claim 48, drawn to a second method of using the composition, classified in class 514, subclass 886.
- IV Claim 49, drawn to a fourth method of using the composition, classified in class 514, subclass 859.
- V Claim 50, drawn to a fifth method of using the composition, classified in class 424, subclass 725.

The applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 9, 18, 26, and 34 are generic.

During a telephone conversation with Wayne Western on 12/10/2001 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-42 and for component I, the alpha-acid, humulone and for component II, the beta-acid, lupulone. This election is affirmed as required by the Examiner. However, reconsideration of the restriction requirement is requested on the grounds that the invention is a unitary invention. The Examiner alleges that Inventions II-V are related as different methods from one another. They are patentably distinct since it is clear that many different methods can use the same composition as is evidenced by the claims themselves. The Examiner states that in the instant case the product can be used in a materially distinct process, such as in the treatment of AIDS. The Examiner alleges Invention I and II-V are related as product and processes of use. They can be used for different processes as is evidenced by the claims themselves and can be used in different processes such as treating diseases, such as AIDS, cancer, etc.


The applicants respectfully disagree because the Examiner submits no evidence showing that the different methods which can use the same composition are materially different processes. The Examiner submits no evidence to support the allegation that they are patentably distinct since it is clear that many different methods can use the same composition as is evidenced by the claims themselves. In addition, the fact that Groups I and V, II-IV are classified in the same classes shows that these groups are similar enough that it would not create an undue burden for the examiner to examine both of these groups concurrently. Therefore, the applicant respectfully requests reconsideration in this matter and withdrawal of this requirement.

REMARKS FOR CLAIM REJECTIONS

Claims 1, 3-6, 8, 11-15, 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Haas, US Patent No.3,932,603(hereafter as "Haas").

The Examiner states that Haas teaches a composition containing hop extract which contains lupulone and humulone and sweeteners. The Examiner also states that Versluys, US Patent 4,401,684(hereafter as "Versluys") clearly shows that hops contain both humulones and lupulones.

It is respectfully submitted that the composition in the amended claims "consist essentially of alpha acids and beta acids in a ratio capable of specifically inhibiting COX-2 activity" are not anticipated by Haas because Haas does not teach every element of the compositions claimed in the present invention. Hop extract resins are listed as one of antimicrobials in Haas. Hop extracts resins are mixtures of many ingredients in addition to alpha acids and beta acids. However, the compositions claimed in the present application "consist essentially of alpha acids and beta acids" which are different from hop extract resins. In addition, Haas does not teach a composition consisting essentially of alpha acids and beta acids in a ratio capable of specifically inhibiting COX-2 activity. Therefore, it is respectfully submitted that Haas does not anticipate the present invention as claimed in the amended claims and the 102 rejection should be withdrawn.



Claims 1-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haas taken with Versluys and Todd, Jr., US Patent 5,073,396 (hereafter as "Todd").

The Examiner indicates that Haas does not teach specific amounts of lupulone and humulone, that the hop is CO₂ extracted and that a vitamin, such as vitamin C, is used in the composition. However, the Examiner alleges that Versluys teaches that vitamin C is used as an

antioxidant to prevent deterioration of the hops. The Examiner also alleges that Todd teaches that the hop in beer is routinely CO₂ extracted. The Examiner then concludes that it would have been obvious for one of ordinary skill in the art to CO₂ extract the hops of Haas since Todd teaches that this is routinely done to hops. The Examiner also concludes that it would have been obvious to use vitamin C in the composition since vitamin C is clearly desirable to use when one wants to keep hops from deteriorating as evidenced by Versluys. The Examiner states that "one would clearly want to prevent the hops from deteriorating thus there is motivation to use the vitamin C." In addition, the Examiner states that "to use the specific amounts of lupulone and humulone also would have been obvious since the adjustment of particular conventional working parameters (e.g., determining result effective amounts of the ingredients beneficially taught by the cited references, especially within the broad ranges instantly claimed), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan." The Examiner concludes that "accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results."

The applicant respectfully traverses. The burden is on the Examiner to establish a case of *prima facie* obviousness. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). In order to do this by combining references, the prior art must provide some reason or motivation to make the claimed compositions, *In re Dillon*, 16 U.S.P.Q.2d 1897, 1901 (Fed. Cir. 1990) (en banc). When making a rejection under 35 U.S.C. § 103 there are three fundamental areas the Examiner is required, under 37 C.F.R. § 1.106 and MPEP § 706.02, to cover. First, the rejection should set forth the differences between the claims and the prior art. Second, the proposed modification of the applied references necessary to arrive at the claimed subject matter should be clearly stated in

the references. Third, there must be an explanation as to why such proposed modifications would be obvious.

In the rejection entered by the Examiner under § 103, there is a flaw which cannot be resolved simply by the Examiner making an allegation that "it would be obvious". There must be some reason, suggestion or motivation in the art cited to combine the references in the manner stated by the Examiner. Were it not for first having read the Applicants' disclosure and then by hindsight application attempting to piece together portions of each reference rather than considering each reference for what it teaches as a whole, it is not believed a rejection would have been entered. With the above background in mind the rejection under 35 U.S.C. § 103 will be discussed.

The present invention relates to discovery of a composition consisting essentially of an alpha acid and a beta acid in a ratio capable of inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity.

Haas discloses improved oral preparations having the effect of inhibiting dental caries in the mouth. In a long list of compounds found to be highly effective as antimicrobials against cariogenic streptococci, hop extract resins are disclosed at the end of the list. See col 2, line 4. However, hop extract resins are mixtures of many ingredients in addition to alpha acids and beta acids. Nothing in Haas teaches or suggests a combination of an alpha acid and a beta acid in a ratio which is capable of inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity. Versluys discloses a method of preserving hops, not a CO₂ extract of hops, from oxidation by adding ascorbic acid to the hops. A CO₂ extract of hops is not likely undergo oxidation since the pro-oxidation compounds in the hops have been removed through extraction. Therefore, Versluys does not teach or suggest a composition consisting essentially of an alpha

acid and a beta acid in a ratio capable of inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity. Todd discloses a beer flavored with an extract which is essentially devoid of alpha and beta acids. Therefore, not only is there nothing in Todd that teaches or suggests a composition consisting essentially of an alpha acid and a beta acid in a ratio capable of inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, but Todd actually teaches away from the present invention by providing an extract which is essentially devoid of alpha and beta acids. In addition, as Haas relates to an oral composition, Versluys relates to a method of preventing oxidation of hops, not a CO₂ extract of hops and Todd relates to a beer with a non-acidic hop-flavored fraction, there is no motivation indicated in any of the cited references to make a combination capable of inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity. Furthermore, even though a combination can be made according to the Examiner, it will not arrive at the composition consisting essentially of an alpha acid and a beta acid in a ratio capable of inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity as claimed in the present application.

Based on the above it is respectfully submitted that the Examiner has not established *prima facie* obviousness for the amended claims based on the references cited. In other words, one of ordinary skill in the art when combining all the knowledge and methods at the time of the invention was made, would not come up with the composition as claimed in the present invention. Thus, the Examiner is respectfully requested to withdraw the rejection.

In conclusion, all the claims in the present application are patentably different from all the references cited in the Examiner's rejection. Therefore, it is respectfully submitted that all the rejections be withdrawn and that all pending claims be allowed and this application be passed to issue.

If any impediment to the allowance of these claims remains, the Examiner is invited to call Dr. Weili Cheng, who is an attorney of record at (801) 566-6633, or in her absence, the undersigned at the same number, so that such matters may be resolved as expeditiously as possible.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment to Deposit Account No. 20-0100.

Dated this 1st day of **Apr.** 2002.

Respectfully submitted,

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1(amended). A composition for consisting essentially of an alpha acid and a beta acid in a ratio that, when administered, is capable of inhibition of inducible COX-2 activity and while having minimal effect on COX-1 activity, ~~said composition comprising an effective amount of component I selected from the group consisting of alpha acids and beta acids and an effective amount of at least one component II selected from the group consisting of alpha acids, beta acids, essential oils, fats and waxes, with the proviso that component I and II are not the same compound.~~

2(amended). The composition of Claim 1 wherein the ~~component I~~alpha acid or Hbeta acid is made from a hop extract prepared by CO₂ extraction.

3(amended). The composition of Claim 1 wherein the alpha ~~acids are~~acid is selected from the group consisting of: humulone, cohumulone, isohumulone, isoprehumulone, hulupone, adhumulone, xanthohumol A and xanthohumol B.

4(amended). The composition of Claim 1 wherein the beta ~~acids are~~acid is selected from the group consisting of lupulone, colupulone, adlupulone, tetrahydroisohumulone, and hexahydrocolupulone,

~~5. The composition of Claim 1 wherein the essential oils are selected from the group consisting of: myrcene, humulene, beta-caryophyllen, undecane-2-on, and 2-methyl-but-3-en-ol.~~

6. The composition of Claim 1 formulated in a pharmaceutically acceptable carrier.

7. The composition of Claim 1, further comprising one or more members selected from the group consisting of antioxidants, vitamins and minerals.

8. The composition of Claim 1, further comprising one or more members selected from the group consisting of proteins, fats, carbohydrates, glucosamine, chondroitin sulfate and amino sugars.

9(amended). A composition for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition ~~comprising~~consisting essentially 30 to 60 percent alpha acids and 15 to 45 percent beta acids.

10. The composition of Claim 9 wherein the alpha acids or the beta acid is from a hop extract prepared by CO₂ extraction.

~~11. The composition of Claim 9 wherein the CO₂ hop extract contains 0 to 6 percent essential oils and 2 to 8 percent fats and waxes.~~

12. The composition of Claim 9 wherein the alpha acids are selected from the group consisting of: humulone, cohumulone, isohumulone, isoprehumulone, hulupone, adhumulone, xanthohumol A and xanthohumol B.

13. The composition of Claim 9 wherein the beta acids are selected from the group consisting of lupulone, colupulone, adlupulone, tetrahydroisohumulone, and hexahydrocolupulone.

~~14. The composition of Claim 11 wherein the essential oils are selected from the group consisting of myrcene, humulene, beta-caryophyllene, undecane-2-one, and 2-methyl-but-3-en-ol.~~

15. The composition of Claim 9 formulated in a pharmaceutically acceptable carrier.

16. The composition of Claim 9, further comprising one or more members selected from the group consisting of antioxidants, vitamins and minerals.

17. The composition of Claim 9, further comprising one or more members selected from the group consisting of proteins, fats, carbohydrates, glucosamine, chondroitin sulfate and amino sugars.

~~18. A composition for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising 30 to 60 percent alpha acids and 3 to 6 percent essential oil.~~

~~19. The composition of Claim 18 wherein the alpha acids or the essential oil is from a hop extract prepared by CO₂ extraction.~~

~~20. The composition of Claim 19 wherein the CO₂ extract of hops contains 2 to 8 percent fats and waxes.~~

~~21. The composition of Claim 18 wherein the alpha acids are selected from the group consisting of humulone, cohumulone, isohumulone, isoprenhumulone, lupulone, adhumulone, xanthohumol A and xanthohumol B.~~

~~22. The composition of Claim 18 wherein the essential oils are selected from the group consisting of myrcene, humulene, beta-caryophyllene, undecane-2-one, and 2-methyl-but-3-en-ol.~~

~~23. The composition of Claim 18 formulated in a pharmaceutically acceptable carrier.~~

~~24. The composition of Claim 23, further comprising one or more members selected from the group consisting of antioxidants, vitamins and minerals.~~

~~25. The composition of Claim 23, further comprising one or more members selected from the group consisting of proteins, fats, carbohydrates, glucosamine, chondroitin sulfate and amino sugars.~~

~~26. A composition for the inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising 15 to 45 percent beta acids and 3 to 6 percent essential oil.~~

~~27. The composition of Claim 26 wherein the beta acids or the essential oil is from a hop extract prepared by CO₂ extraction.~~

~~28. The composition of Claim 27 wherein the CO₂-extract of hops contains 2 to 8 percent fats and waxes.~~

~~29. The composition of Claim 26 wherein the beta acids are selected from the group consisting of lupulone, colupulone, adlupulone, tetrahydroisohumulone, and hexahydrocolupulone~~

~~30. The composition of Claim 26 wherein the essential oils are selected from the group consisting of: myrcene, humulene, beta-caryophyllen, undecane-2-on, and 2-methyl-but-3-en-ol.~~

~~31. The composition of Claim 26 formulated in a pharmaceutically acceptable carrier.~~

~~32. The composition of Claim 31, further comprising one or more members selected from the group consisting of antioxidants, vitamins and minerals.~~

~~33. The composition of Claim 31, further comprising one or more members selected from the group consisting of proteins, fats, carbohydrates, glucosamine, chondroitin sulfate and amino sugars.~~

~~34. A composition for the inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising 30 to 60 percent alpha acids, 15 to 45 percent beta acids and 3 to 6 percent essential oil.~~

~~35. The composition of Claim 34 wherein the alpha acids, beta acids or the essential oil is from a hop extract prepared by CO₂-extraction.~~

~~36. The composition of Claim 34 wherein the CO₂-extract of hops contains 2 to 8 percent fats and waxes.~~

~~37. The composition of Claim 34 wherein the alpha acids are selected from the group consisting of: humulone, cohumulone, isohumulone, isoprehumulone, hulupone, adhumulone, xanthohumol A and xanthohumol B.~~

~~38. The composition of Claim 34 wherein the beta acids are selected from the group consisting of: lupulone, colupulone, adlupulone, tetrahydroisohumulone, and hexahydrocolupulone,~~

~~39. The composition of Claim 34 wherein the essential oils are selected from the group consisting of: myrcene, humulene, beta-caryophyllen, undecane-2-on, and 2-methyl-but-3-en-ol.~~

~~40. The composition of Claim 34 is formulated in a pharmaceutically acceptable carrier.~~

~~41. The composition of Claim 40, further comprising one or more members selected from the group consisting of antioxidants, vitamins and minerals.~~

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~~42. The composition of Claim 41, further comprising one or more members selected from~~

~~the group consisting of proteins, fats, carbohydrates, glucosamine, chondroitin sulfate and amino sugars.~~

~~43. A method of dietary supplementation in animals comprising administering to an animal suffering symptoms of inflammation a composition for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising an effective amount of component I selected from the group consisting of alpha acids and beta acids and an effective amount of at least one component II selected from the group consisting of alpha acids, beta acids, essential oils, fats and waxes, with the proviso that component I and II are not the same compound.~~